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Award Number:
W81XWH-07-1-0269

TITLE:
Biomarkers of Risk for Post-traumatic Stress Disorder (PTSD)

PRINCIPAL INVESTIGATOR:
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REPORT DATE:
Rá] 2009

TYPE OF REPORT:
Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE 01-05-2009		2. REPORT TYPE Annual		3. DATES COVERED 04/02/2008-04/01/2009	
4. TITLE AND SUBTITLE Biomarkers of Risk for Post-traumatic Stress Disorder (PTSD)				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-07-1-0269	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Audrey R. Tyrka, M.D., Ph.D. Email: audrey_tyrka@brown.edu				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Butler Hospital Providence, RI 02906				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT The objective of this proposal is to study genetic and neuroendocrine biomarkers of risk in a carefully assessed population of military personnel who have recently returned from war zones. The target sample includes 300 men and women who have recently returned from hazardous deployment and are undergoing a comprehensive assessment of symptoms and stressors in a related 12-month longitudinal study. To date, we have enrolled 203 subjects. Samples of saliva have been obtained from all 203 enrolled subjects for analysis of DNA and candidate genes. Cortisol samples have been obtained from 157 of these subjects. Hormone and genetic data will be used to predict the development of PTSD and chronic PTSD. In addition, interactions of these biomarkers with trauma severity and other stressors as well as social supports will be examined.					
15. SUBJECT TERMS PTSD, trauma, genetics, cortisol, biological marker, risk factors					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 23	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

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Introduction

Experience from prior military conflicts and early data from Iraq and Afghanistan suggest that a significant percentage of troops on hazardous deployments will develop posttraumatic stress disorder (PTSD). This is one of the most common, debilitating, and chronic psychological disorders diagnosed among veterans. A large body of evidence in PTSD now documents dysfunction of the hormone system that coordinates the biological response to stress (the hypothalamic-pituitary-adrenal [HPA] axis). However, existing studies typically involve participants who have suffered from the disorder for many years, and information on biological processes occurring early in the disorder is lacking. In addition, specific genes that regulate HPA axis function have recently been identified in humans. Genes that are involved in the processing of emotions and cognition may also be involved in the pathogenesis of PTSD. In recent years investigators have begun to identify some of the relevant genes, and a few recent studies have identified specific gene-environment interactions that appear to confer risk for mood and anxiety disorders. The objective of this proposal is to study these biomarkers of risk in a carefully assessed population of military personnel who have recently returned from war zones. This study will enroll a target sample of 300 men and women who have recently returned from hazardous deployment in a war zone and are undergoing a comprehensive assessment of symptoms and stressors in a related 12-month longitudinal study. Samples of saliva will be obtained for analysis of DNA and candidate genes as well as hormone concentrations (cortisol). Hormone and genetic data will be used to predict the development of PTSD and chronic PTSD. In addition, interactions of trauma severity and other stressors as well as social supports with the biological factors will be examined. Findings of this study will contribute to knowledge about the biomarkers of risk for PTSD and will therefore increase our knowledge of the disease process and may help us to identify individuals who are at highest risk for PTSD.

Body

This year we consented 78 subjects who were eligible for the study and collected genetics samples on all of them. We received salivary cortisol back from 61 subjects this year. All specimens have been catalogued, processed, and stored. All collection materials have been ordered. We renewed our IRB approval. We started running assays and analyses will be done in year of the grant.

Key Research Accomplishments

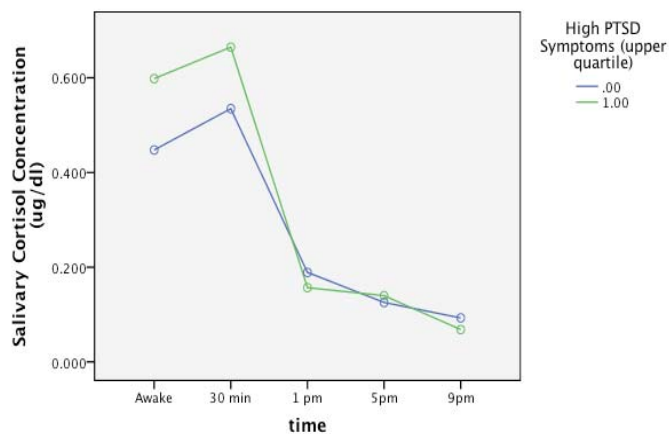
- Total consented subjects: 203
- Total collected genetic samples: 203 subjects
- Total collected salivary cortisol: 157 subjects
- Processed and stored all specimens

- Started to run assays and do preliminary analyses
- Started to clean data
- Renewed IRB approval

Reportable Outcomes

The data presented below reflect preliminary analyses with the available data.

Cortisol: Cortisol data for 93 subjects are available presently for analysis. A repeated measures analysis of the effects of trauma exposure (Hoge scale) and current PTSD symptoms, controlling for effects of age, showed a significant effect of PTSD symptoms over time ($F(4, 85) = 2.95$, $p=.025$) and a significant interaction of PTSD symptoms and trauma exposure over time ($F(4, 85) = 6.85$, $p<.001$). As shown in the figure to the right, among subjects with moderate trauma exposure (Hoge score at or above the median of 10), those with PTSD symptoms had higher cortisol concentrations upon awakening and 30-minutes following awakening.



Genetics: Preliminary data -genetics: We have extracted DNA samples from the first 148 samples and genotyped them for the 5HTTLPR (triallelic data), COMT rs4680 SNP and, DAT VNTR. Genotype frequencies were SS: $n = 33$ (22.3%), SLG: $n = 0$ (0%), LGLG: $n = 0$ (0%), SLA: $n = 74$ (50%), LGLA: $n = 9$ (6.1%), and LALA: $n = 32$ (21.6%). COMT rs4680 genotype frequencies were: Met/Met: $n = 37$ (32%), Val/Met: $n = 51$ (44.7%), Val/Val: $n = 26$ (23%). DAT VNTR genotype frequencies were: 9/9: $n = 10$ (6.7%), 10/9: $n = 60$ (40.5%), 10/10: $n = 78$ (52.7%). Initial analyses did not reveal any significant associations between genotype and PTSD diagnosis. This may be due to insufficient power, so the next steps will be to genotype additional samples. Further analyses will examine the importance of comorbid diagnoses, degree of trauma exposure, and will include potentially critical covariates such as childhood maltreatment.

Conclusion

Recruitment and collection of genetic and salivary cortisol specimens has been proceeding according to timeline. We have started to run assays, clean data and will run final analysis in year3.

References

N/A

Appendix

Dr. Tyrka's CV is attached.

Supporting Data

N/A

CURRICULUM VITAE
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EDUCATION

Undergraduate: State University of New York College at Purchase, Purchase, NY, B.A. Psychology,
1988.

Pre-Medical: State University of New York College at Purchase, Purchase, NY, pre-medical
coursework, 1989-1991.

Columbia University, School of General Studies, New York, NY, Pre-Medical
Certificate, 1992

Medical School: University of Pennsylvania School of Medicine, Philadelphia, PA, M.D., 1999,
(combined M.D.-Ph.D. program, 1992-1999)

Graduate School: University of Pennsylvania, Department of Psychology, Philadelphia, PA, Ph.D.,
Psychology, 1999 (combined M.D.-Ph.D. program, 1992-1999)

PREDOCTORAL FELLOWSHIPS

1993-1994 Medical Scientist Training Program

1994-1999 NIMH National Research Service Award

POSTGRADUATE TRAINING

Residency: Resident in Psychiatry, Brown University School of Medicine, Providence, RI, 1999-
2003.

Research Track, Psychiatry Residency and the Mood Disorders Research Program and
Laboratory for Clinical Neuroscience, Butler Hospital and Brown University, 2001-2003.

PREDOCTORAL HONORS AND AWARDS

1988 B.A., Summa Cum Laude, State University of New York College at Purchase

1988 Award for Outstanding Undergraduate Research, State University of New York

1994 Robert M. Toll Psychiatry Research Prize, University of Pennsylvania

- 1999 AMA Rock Sleyster Memorial Scholarship
- 1999 Kenneth E. Appel Psychiatry Award, University of Pennsylvania School of Medicine

POSTGRADUATE HONORS AND AWARDS

- 2002 The American College of Psychiatrists 2002 Laughlin Fellowship Recipient.
- 2002 First Prize, Resident Research, Sixth Annual Research Symposium, Brown University School of Medicine Department of Psychiatry and Human Behavior
- 2003 American Psychiatric Association Research Colloquium for Junior Investigators, Participant and Travel Award Recipient
- 2003 NIMH Mentored Patient-Oriented Research Career Development Award
- 2003 Janssen Psychiatry Resident Award of Excellence
- 2003 NARSAD Young Investigator Award
- 2003 Janssen Pharmaceutica Faculty Development Award in Psychopharmacology
- 2003 NIH Clinical Research Loan Repayment Program
- 2004 American College of Neuropsychopharmacology Young Investigator Travel Award
- 2005 Future Leaders in Psychiatry Symposium Travel Award
- 2007 Outstanding Teaching Award in General Psychiatry, Warren Alpert Medical School of Brown University, Department of Psychiatry and Human Behavior

PROFESSIONAL LICENSES AND BOARD CERTIFICATION

- Diplomate, National Board of Medical Examiners, 2000.
- Licensed Medical Doctor, Board of Medical Licensure and Discipline, State of Rhode Island and Providence Plantations, 2003.
- Diplomate, American Board of Psychiatry and Neurology, 2004.

ACADEMIC APPOINTMENTS

- Assistant Professor of Psychiatry and Human Behavior, Brown Medical School, Providence, RI, 7/03-
- Associate Chief, Mood Disorders Program, Butler Hospital, 7/03-

HOSPITAL APPOINTMENTS

Attending Psychiatrist, Butler Hospital, 2003-

Attending Psychiatrist, Kent County Memorial Hospital, Providence, RI 2003-

Assistant Unit Chief, General Treatment Unit Delmonico 4, Butler Hospital, 2005-2007

OTHER APPOINTMENTS

Editorial Board Member, Acta Psychiatrica Scandinavica, 2007-

Director, Trainee Editorial Board, Acta Psychiatrica Scandinavica, 2007-

Grant Reviewer, Special Emphasis Panel “NIMH Centers for Pediatric Mental Health.” ZMH1-ERB-A-05

Grant Reviewer, Special Emphasis Panel Department of Defense PTSD/TBI Post Traumatic Stress Disorder
Intramural #2

Ad Hoc Reviewer: American Journal of Psychiatry
Archives of General Psychiatry
Biological Psychiatry
Bipolar Disorders
Developmental Psychobiology
European Neuropsychopharmacology
Journal of Abnormal Psychology
Journal of Adolescent Health
Journal of Affective Disorders
Molecular Psychiatry
Neuropsychopharmacology
Pediatrics
Psychiatry Research
Psychological Medicine
Psychoneuroendocrinology
Psychopharmacology
Psychophysiology

HOSPITAL COMMITTEES

Butler Hospital Unit Leadership 2003-2006

Butler Hospital Physician’s Subcommittee: Improvement of Organizational Performance 2004-

Butler Hospital President’s Leadership Work Group 2007-

Butler Hospital Committee on Ethnic Diversity in Research Participation, 2006-2007

Butler Hospital Committee on Staff Wellness Programs 2008-

UNIVERSITY COMMITTEES

Brown Medical School: Medical Curriculum Committee, Subcommittee on Years 3 and 4, 2004-6

MEMBERSHIPS IN SOCIETIES

American Psychiatric Association 1989-

Rhode Island Psychiatric Society, 2004-

Society of Biological Psychiatry, 2005-

American College of Neuropsychopharmacology Associate Member, 2007-

ORIGINAL PUBLICATIONS IN PEER-REVIEWED JOURNALS

1. **Tyrka, A.** and Smith, G.P. Potency of SCH 23390 for decreasing sucrose intake in rat pups depends on mode of ingestion. Pharmacology Biochemistry & Behavior, 39(4):955-961, 1991.
2. Smith, G.P., **Tyrka, A.** and Gibbs, J. Type-A CCK receptors mediate the inhibition of food intake and activity by CCK-8 in 9- to 12-day-old rat pups. Pharmacology Biochemistry & Behavior, 38(1):207-210, 1991.
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9. Carpenter, L.L., Heninger, G.R., McDougle, C.J., **Tyrka, A.R.**, Epperson, C.N., Price, L.H. Cerebrospinal fluid interleukin (IL)-6 in obsessive-compulsive disorder and trichotillomania. Psychiatry Research, 112 (3) 257-262, 2002.
10. Graber, J.A., **Tyrka, A.R.**, and Brooks-Gunn, J. How similar are different subclinical eating problems and bulimia nervosa? Journal of Child Psychology and Psychiatry, 44 (2) 262-273, 2003.

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6. Price, L.H., Carpenter, L.L., **Tyrka, A.R.** Lithium augmentation for refractory depression: A critical reappraisal. *Primary Psychiatry*, 15(11), 35-42, 2008.

BOOKS AND BOOK CHAPTERS

1. **Tyrka, A.R.**, Haslam, N., and Cannon, T. D. Detection of a latent taxon of individuals at-risk for schizophrenia-spectrum disorders. In A. Raine, T. Lencz, and S.A. Mednick (Eds), *Schizotypal Personality*, New York: Cambridge University Press, pp 168-191, 1995.
2. **Tyrka, A.R.**, Graber, J.A., and Brooks-Gunn, J. The development of disordered eating:

Correlates and predictors of eating problems in the context of adolescence. In M Lewis, AJ Sameroff, and SM Miller (Eds), *Handbook of Developmental Psychopathology, 2nd Ed.*, New York: Kluwer Academic/ Plenum Publishers, 2000.

3. **Tyrka, A.R.**, Wier, L.M. Eating disorders. In K.A. McGarry and I.L. Tong (Eds), *5-Minute Consult Clinical Companion to Women's Health*, Philadelphia: Lippincott Williams & Williams, pp. 96-96, 2007.
4. **Tyrka, A.R.**, Carvalho, J.P.. Depression. In K.A. McGarry and I.L. Tong (Eds), *5-Minute Consult Clinical Companion to Women's Health*, Philadelphia: Lippincott Williams & Williams, pp. 82-84, 2007.
5. **Tyrka, A.R.**, Wyche, M.C.. Anxiety Disorders. In K.A. McGarry and I. Tong (Eds), *5-Minute Consult Clinical Companion to Women's Health*, Philadelphia: Lippincott Williams & Williams, pp. 25-27, 2007.

OTHER NON PEER REVIEWED PUBLICATIONS

Price, L.H., **Tyrka, A.R.** Letter to the Editor Re: Adjunctive antidepressant treatment for bipolar depression. New England Journal of Medicine, 357, p 614, 2007.

PUBLICATIONS IN PREPARATION

1. **Tyrka, A.R.**, Kelly, M.M., Graber, J.A., Ross, N.S., Warren, M.P. and Brooks-Gunn, J Neuroendocrine Predictors of behavioral adjustment in boys: A prospective longitudinal study of a community sample. In preparation.
2. **Tyrka, A.R.**, Price, L.H., Kao, H.T., Porton, B., Marsella, S.A., and Carpenter, L.L. Childhood Maltreatment and Telomere Shortening: Preliminary Support for an Effect of Early Stress on Cellular Aging, submitted to Biological Psychiatry.
3. Carpenter, L.L., Carvalho, J., Kelly, M.M., **Tyrka, A.R.**, and Price, L.H. Does a history of childhood maltreatment influence recall of responses to a psychosocial stress task? In preparation.
4. Carpenter, LL., **Tyrka, AR**, Tracy, AP, Wilkinson, CW, and Price, LH. Leviteracetam lowers cortisol response to the Dex/CRH test in healthy adults with high baseline cortisol reactivity, in preparation.

ABSTRACTS

- A1. **Tyrka, A.**, Smith, G.P., and Gibbs, J. SCH 23390 inhibits intake of sucrose more during independent ingestion than during intraoral infusion in rats as early as postnatal day 7. Society for Neuroscience, 1990.

- A2. Broder, L., Smith, G.P., **Tyrka, A.**, and Gibbs, J. Independent ingestion and intraoral infusion of 10% sucrose produce different patterns of central dopamine metabolism in 14-day-old rats. Society for Neuroscience, 1990.
- A3. **Tyrka, A.**, and Smith, G.P. Is density of reinforcement responsible for the differential effect of DA antagonists on rat pups during two ingestion tests? Society for Neuroscience, 1991.
- A4. **Tyrka, A.R.**, Gibbs, J., and Smith, G.P. SCH 23390, but not raclopride, decreases intake of intraorally infused 10% sucrose in adult rats. Society for the Study of Ingestive Behavior, 1991.
- A5. **Tyrka, A.R.**, Waldron, I., Graber, J.A. and Brooks-Gunn, J. Prospective predictors of the development of eating disorders in a community sample of young women. University of Pennsylvania Annual Research Symposium, April, 1999.
- A6. Carpenter L. L., **Tyrka A.R.**, Price L. H. Cerebrospinal Fluid (CSF) Interleukin-6 in depressed patients and healthy controls. Sixth Annual Brown University Research Symposium, March 2002.
- A7. **Tyrka A. R.**, Carpenter L. L., Anderson G. A., Brown R., Price L. H. Relationship between early life stress and pituitary-adrenal function as measured by the dexamethasone/corticotrophin releasing hormone test. Sixth Annual Brown University Research Symposium, March 2002.
- A8. **Tyrka, A. R.**, Carpenter, L.L., Brown, R.A., Strong, D.R., Kahler, C.W., Anderson, G.M., Price, L.H. Early-Life Stress and Response to the Dexamethasone/Corticotropin-Releasing Hormone Test in Healthy Adults. Annual Meeting of the American College of Neuropsychopharmacology, December 2002.
- A9. Carpenter L. L., **Tyrka A. R.**, Schecter J., Haggarty R., and Price L. H. Tiagabine (gabitril) for major depressive disorder with anxiety. Seventh Annual Brown University Research Symposium, March 2003.
- A10. Carpenter, L. L., **Tyrka A. R.**, Stout, S. C., Owens, M. J., Nemeroff, C. B., and Price, L. H. Elevated cerebrospinal fluid (CSF) concentrations of substance p in major depression. Seventh Annual Brown University Research Symposium, March 2003.
- A11. **Tyrka A. R.**, Price L. H., Owens M. J., Nemeroff C. B., and Carpenter L. L. Cerebrospinal fluid corticotropin-releasing factor following oral paroxetine in adults with depression and perceived early-life stress. Seventh Annual Brown University Research Symposium, March 2003.
- A12. Carpenter LL, **Tyrka AR**, Schecter J, Haggerty R, Lawrence Price MD. An open-label trial of tiagabine for major depressive disorder with anxiety. Society for Biological Psychiatry Annual Meeting, #107, May, 2003.
- A13. Carpenter. L.L., **Tyrka, A.R.**, Schecter, J., Haggarty, R., and Price, L.H. Tiagabine for MDD with anxiety. American Psychiatric Association Ann Mtg, #NR501, May 2003.
- A14. **Tyrka, A.R.**, Carpenter, L.L., Brown, R.A., Strong, D.R., Kahler, C.W., Anderson, G.M., and Price, L.H. Early-Life Stress And Response To The Dexamethasone/Corticotropin-Releasing Hormone Test In Healthy Adults. Society for Biological Psychiatry Annual Meeting, #145, May, 2003.

- A15. **Tyrka, A.R.**, Carpenter, L.L., Brown, R.A., Strong, D.R., Kahler, C.W., Anderson, G.M., and Price, L.H. Early-Life Stress and Pituitary-Adrenal Function in Healthy Adults. American Psychiatric Association Annual Meeting, #NR61, May, 2003.
- A16. Carpenter LL, **Tyrka AR**, Schecter J, Haggerty R, Lawrence Price MD. An open-label trial of tiagabine for major depressive disorder with anxiety. Institute on Psychiatric Services, 2003.
- A17. **Tyrka, A.R.**, Carpenter, L.L., McDougale, C.J., Kirwin, P.D., Owens, M.J., Nemeroff, C.B., and Price, L.H. CSF Corticotropin-releasing factor increases during tryptophan depletion. Eighth Annual Brown University Research Symposium, March 2004.
- A18. **Tyrka, A.R.**, Carpenter, L.L., McDougale, C.J., Kirwin, P.D., Owens, M.J., Nemeroff, C.B., and Price, L.H. CSF Corticotropin-releasing factor increases during tryptophan depletion. American Psychiatric Association Annual Meeting, #NR78, May 2004.
- A19. Greenberg, B.D., Price, L.H., Friehs, G., Malone, D., Rezai, A.R., Shapira, N.A., Foote, K.D., Okun, M.A., Rauch, S.L., Dougherty, D., Noren, G., Malloy, P.F., Salloway, S., Marsland, R., **Tyrka, A.**, Carpenter, L., Goodman, W., and Rasmussen, S.A. Deep Brain Stimulation in Intractable OCD, and Preliminary Results in Intractable Depression. 44th Annual Meeting of the New Clinical Drug Evaluation Unit (NCDEU), June, 2004.
- A20. Grover, K.E., **Tyrka, A.R.**, Carpenter, L.L., Mello, A.A.F., Mello, M.F., Gagne, G.G., and Price, L.H. Personality and hypothalamic-pituitary-adrenal function in healthy adults. Rhode Island Hospital 12th Annual Hospital Research Celebration, October, 2004.
- A21. Greenberg BD, Friehs G, Carpenter L, **Tyrka A**, Malone D, Rezai A, Shapira N, Foote K, Okun M, Goodman W, Rasmussen S, **Price LH**. Deep brain stimulation: Clinical findings in intractable depression and OCD. Abstr Amer Coll Neuropsychopharm #468, December, 2004.A21.
- A22. **Tyrka, A.R.**, Carpenter, L.L., Feijo do Mello, A.A., Feijo de Mello, M., Gagne, G.G., Grover, K.E., and Price, L.H. Temperament and Pituitary-Adrenal Response to the DEX/CRH Test in Healthy Adults. Annual Meeting of the American College of Neuropsychopharmacology, December 2004.
- A23. Carpenter L.L., **Tyrka, A.R.**, Carvalho, J., Wier, L. Gagne, G., Mello, A.F., Mello, M.F., and Price, L.H. Decreased cortisol response to the trier social stress test in healthy adults with significant childhood adversity. Ninth Annual Brown University Research Symposium, March 2005.
- A24. Rikhye, K. Carpenter, L.L, **Tyrka, A.R.**, Gagne, G, Feijo de Mello, A.A., Feijo de Mello, M., Price, L.H. Interplay between childhood adversity, parental bonding, and sex effects: Impact on quality of life. Ninth Annual Brown University Research Symposium, March 2005.
- A25. **Tyrka, A.R.**, Carpenter, L.L., Feijo de Mello, A.A., Feijo de Mello, M., Gagne, G.G., Grover, K.E., Anderson, G.M., and Price, L.H. Temperament and Pituitary-Adrenal Response to the DEX/CRH Test in Healthy Adults. Ninth Annual Brown University Research Symposium, March 2005.

- A26. Grover, K.E., **Tyrka, A.R.**, Carpenter, L.L., Gagne, G.G., Feijo de Mello, A.A., Feijo de Mello, M., and Price, L.H. The Relationship between Childhood Abuse and Adult Personality Disorder Symptoms. Ninth Annual Brown University Research Symposium, March 2005.
- A27. **Tyrka, A.R.**, Carpenter, L.L., Feijo de Mello, A.A., Feijo de Mello, M., Gagne, G.G., Grover, K.E., Anderson, G.M., and Price, L.H. Temperament and Pituitary-Adrenal Response to the DEX/CRH Test in Healthy Adults. Annual Meeting of the Society of Biological Psychiatry, May, 2005.
- A28. **Tyrka, A.R.**, Carpenter, L.L., Wier, L.M., Mello, A.F., Mello, M.F., Gagne, G.G., Grover, K.E., Anderson, G.M., and Price, L.H. Temperament and Response to the Dex/CRH Test in Healthy Adults. 36th Annual Conference of the International Society of Psychoneuroendocrinology, September, 2005.
- A29. Carpenter, L.L., **Tyrka, A.R.**, Carvalho, J.P., Wier, L.M., Gagne, G.G., Mello, A.F., Mello, M.F., Anderson, G.M., and Price, L.H. Decreased Cortisol Response to the Trier Social Stress Test in Healthy Adults with Significant Childhood Adversity. 36th Annual Conference of the International Society of Psychoneuroendocrinology, September, 2005.
- A30. Wier, L.M., **Tyrka, A.R.**, Carpenter, L.L., Carvalho, J., Rikhye, K., Anderson, G.M., and Price, L.H. Stress-Reactive Temperaments and Cortisol Response to the Dex/CRH Test in Healthy Adults. Rhode Island Hospital Thirteenth Annual Research Celebration, Providence, RI, September, 2005.
- A31. Carvalho, John P., **Tyrka, A.R.**, Wier, L.M., Gagne, G.G., Mello, A.F., Mello, M.F., Anderson, G.M., Price, L.H., and Carpenter, L.L. The Relationship Between Childhood Adversity and Stress Responsivity. Rhode Island Hospital Thirteenth Annual Research Celebration, Providence, RI, September, 2005.
- A32. **Tyrka, A.R.**, Carpenter, L.L., Wier, L.M., Wilkinson, C.W., Anderson, G.M., and Price, L.H. Inhibited Temperament and HPA Axis Function in Healthy Adults. Annual Meeting of the American College of Neuropsychopharmacology, December 2005.
- A33. Carpenter, L.L., **Tyrka, A.R.**, Carvalho, J.P., Wier, L., Gagne, G.G., Mello, A.F., Mello, M.F., Anderson, G.M., Wilkinson, C.W., and Price, L.H. Cortisol Response to the Trier Social Stress Test in Healthy Adults with Significant Childhood Adversity. Annual Meeting of the American College of Neuropsychopharmacology, December 2005.
- A34. Kelly, M. M., Carpenter, L. L., **Tyrka, A. R.**, Anderson, G., M., & Price, L. H. Parental bonding and stress reactivity: The mediating effects of trait anxiety. 26th annual meeting of the Anxiety Disorders Association of America, Miami, FL, March 2006.
- A35. Carvalho, J.P., **Tyrka, A.R.**, Rikhye, K., Price, L., and Carpenter, L.L. Does a History of Abuse Influence Recall of Psychobiological Responses to a Standardized Stress Test? Tenth Annual Brown University Research Symposium, April 2006.
- A36. Carpenter, L.L., Carvalho, J.P., **Tyrka, A.R.**, Wier, L.M., Gagne, G.G., Mello, A.F., Mello, M.F., Anderson, G.M., Wilkinson, C.W., and Price, L.H. Decreased Cortisol Response to the Trier Social Stress Test in Healthy Adults with Significant Childhood Adversity. Tenth Annual Brown University Research Symposium, April 2006.

- A37. **Tyrka, A.R.**, Carpenter, L.L., Wier, L.M., Wilkinson, C.W., Anderson, G.M., and Price, L.H. Inhibited Temperament and HPA Axis Function in Healthy Adults. Tenth Annual Brown University Research Symposium, April 2006.
- A38. Wyche, M.C, **Tyrka, A.R.**, Kelly, M.M., Wier, L.M., Carvalho, J.P., Rikhye, R., Price, L.H., and Carpenter, L.L. Childhood Abuse and Adult Personality: Does Type of Maltreatment Matter? Tenth Annual Brown University Research Symposium, April 2006.
- A39. Wier, L.M., Carpenter, L.L., Carvalho, J.P., Rikhye, K., Wyche, M.C., Price, L.H., and **Tyrka, A.R.** The Relationship Between Childhood Parental Loss and Adult Psychological Function. Tenth Annual Brown University Research Symposium, April 2006.
- A40. Kelly, M.M., Carpenter, L.L, **Tyrka, A.R.**, Anderson, G.M., and Price, L.H. Parental Bonding and Stress Reactivity: The Mediating Effects of Trait Anxiety. Tenth Annual Brown University Research Symposium, April 2006.
- A41. Kelly, M.M., **Tyrka, A.R.**, Anderson, G.M., Price, L.H., and Carpenter, L.L. Sex Differences in Emotional and Physiological Responses to the Trier Social Stress Test. Tenth Annual Brown University Research Symposium, April 2006.
- A42. **Tyrka, A.R.**, Carvalho, J.P., Wier, L.M., Gagne, G.G., Mello, A.F., Mello, M.F., Anderson, G.M., Wilkinson, C.W., Price, L.W., and Carpenter, L.L. Attenuated cortisol and ACTH responses to the Trier Social Stress Test in healthy adults with a history of childhood maltreatment. Annual Meeting of the Society of Biological Psychiatry, May, 2006.
- A43. Kelly, M. M., **Tyrka, A. R.**, Anderson, G. M., Price, L. & Carpenter, L. L. Sex differences in emotional and physiological responses to the Trier Social Stress Test. 40th annual meeting of the Association for Behavioral and Cognitive Therapies, Chicago, IL., November 2006.
- A44. Wyche, M.C., **Tyrka, A.R.**, Kelly, M.M., Wier, L.M., Carvalho, J.P., Rikhye, K., and Price, L.H., and Carpenter LL. Childhood Abuse and Adult Personality: Does Type of Maltreatment Matter? 14th Annual Research Celebration, Rhode Island Hospital, Providence, RI. November 9, 2006.
- A45. Wier, L.M., Carpenter, L.L., Carvalho, J.P., Rikhye, K., Wyche, M.C., Price, L.H., and **Tyrka, A.R.** The Relationship Between Childhood Parental Loss and Adult Psychological Function. 14th Annual Research Celebration, Rhode Island Hospital, Providence, RI. November 9, 2006.
- A46. **Tyrka, A.R.**, Carpenter, L.L, Gelernter, J., Kelly, M.M., and Price, L.H. COMT genetic variation and depression: gene-environment interaction and HPA axis correlates. Annual Meeting of the American College of Neuropsychopharmacology, December 2006.
- A47. Kelly, M. M., **Tyrka, A. R.**, Graber, J. A., Warren, M., Brooks-Gunn, J. Associations of internalizing and externalizing symptoms with HPA axis stress reactivity in a longitudinal study of boys. Annual Meeting of the American Psychopathological Association, March, 2007

- A48. Wier, W., Carpenter, L.L., Price, L.H., Ross, N., Anderson, G.M., Wilkinson, C.W., and **Tyrka, A.R.** Parental loss in childhood and pituitary-adrenal response to the dexamethasone/corticotropin-releasing hormone test in healthy adults. Eleventh Annual Brown University Research Symposium, April 2007.
- A49. Ross, N., **Tyrka, A.R.**, Price, L.H., Anderson, G.M., and Carpenter, L.L. Childhood maltreatment, female sex, and perceived stress burden: significant determinants of cortisol response to the Dex/CRH test in healthy adults. Eleventh Annual Brown University Research Symposium, April 2007.
- A50. **Tyrka, A.R.**, Carpenter, L.L., Gelernter, J., Kelly, M.M., and Price, L.H. COMT genetic variation and depression: gene-environment interaction and HPA axis correlates. Eleventh Annual Brown University Research Symposium, April 2007.
- A51. Wyche, M.C., Tyrka, A.R., Kelly, M.M., Graber, J.A., Warren, M.P., and Brooks-Gunn, J. Associations of Internalizing and Externalizing Symptoms with HPA Axis Stress Reactivity in a Longitudinal Study of Boys. Eleventh Annual Brown University Research Symposium, April 2007.
- A52. Carpenter, L.L., Ross, N.S., **Tyrka, A.R.**, Mello, A.F., Mello, M.F., Anderson, G.M., Wilkinson, C.W., and Price, L.H. Childhood abuse, depression and gender are significant determinants of cortisol and ACTH response to the dex/crh test. Annual Meeting of the Society of Biological Psychiatry, May, 2007.
- A53. **Tyrka, A.R.**, Carpenter, L.L., Gelernter, J., Kelly, M.M., and Price, L.H. COMT genetic variation and depression: gene-environment interaction and HPA axis correlates. Annual Meeting of the Society of Biological Psychiatry, May, 2007.
- A54. **Tyrka, A.R.**, Wier, L., Price, L.H., Anderson, G., and Carpenter, L.L. Childhood parental loss and cortisol response to the dexamethasone/corticotropin-releasing hormone test in healthy adults. Annual Meeting of the Society of Biological Psychiatry, May, 2007.
- A55. Kelly, M. M., **Tyrka, A. R.**, Price, L. H., & Carpenter, L. L. Sex differences in the use of coping strategies: Predictors of anxiety and depressive symptoms. 41st Annual Meeting of the Association for Behavioral and Cognitive Therapies, Philadelphia, PA, November, 2007.
- A56. Dougherty, D.D., Malone, D., Carpenter, L., **Tyrka, A.**, Friehs, G., Rezai, A. Eskander, E., Machado, A., Kubu, C., Malloy, P., Salloway, S., Rauch, S.L., Price, L., Rasmussen, S. Greenberg, B. Long-term outcomes of ventral capsule/ventral striatum DBS for highly treatment-resistant depression. Annual Meeting of the American College of Neuropsychopharmacology, December 2007.
- A57. **Tyrka, A.R.**, Carpenter, L.L., Gelernter, J., Price, L.H. Serotonin transporter polymorphism, childhood maltreatment, and cortisol response to the Dex/CRH test in healthy adults: Preliminary findings. Annual Meeting of the American College of Neuropsychopharmacology, December 2007.
- A58. Carpenter, L.L., **Tyrka, A.R.**, Anderson, G.M., Wilkinson, C.W., Price, L.H. Depression, childhood maltreatment, and gender are significant determinants of cortisol response to the Dex/CRH test. Annual Meeting of the American College of Neuropsychopharmacology, December 2007.

- A59. Carpenter, L.L., Malone, D.A. Jr, Dougherty, D.A., Rezai, A.R., Friehs, G.M., Eskandar, E.N., Rauch, S.L., Rasmussen, S.A., Machado, A.G., Kubu, C.S., **Tyrka, A.R.**, Price, L.H, Stypulkowski P.H., Giftakis, J.E., Rise, M.T., Malloy, P.F., Salloway, S.P., Greenberg, B.D. Deep Brain Stimulation (DBS) of the Ventral Capsule/Ventral Striatum for Treatment Resistant Major Depression. Twelfth Annual Brown University Research Symposium March, 2008.
- A60. Carpenter, L.L., Price, L.H, Gelernter, J., Ross, N.S., Anderson, G., **Tyrka, A.R.** Serotonin transporter polymorphism, childhood maltreatment, and cortisol response to the Dex/CRH test in healthy adults: Preliminary findings. Twelfth Annual Brown University Research Symposium March, 2008.
- A61. **Tyrka, A.R.**, Price, L.H., Gelernter, J., Anderson, G., Tracy, A.P., Carpenter, L.L. Corticotropin releasing hormone receptor (CRHR1) polymorphisms interact with early life stress to influence the cortisol response to the Dex/CRH test. Twelfth Annual Brown University Research Symposium March, 2008.
- A62. Khoury, L.M., Carpenter, L.L., Price, L.H., Anderson, G., **Tyrka, A.R.** Early life stress and HPA axis function. Twelfth Annual Brown University Research Symposium March, 2008.
- A63. Philip, N.S., Carpenter, L.L., Tyrka, A.R., Price, L.H. Depression and suicidality in outpatients during varenicline (Chantix) treatment: A preliminary report. Twelfth Annual Brown University Research Symposium March, 2008.
- A64. Schoedl AF, Costa MCP, **Tyrka AR**, Carpenter LL, Price LH, Mari JJ, Feijo Melo M. The clinical correlates of reported childhood sexual abuse: An association between age at trauma onset and severity of depression and PTSD in adults. International Symposium on Violence and Mental Health #71, p 51, June, 2008.
- A65. Cui D.H., Zhang H.P., Kranzler H.R., Blumberg H.P., **Tyrka A.R.**, Yang B.Z., Wei F., Carpenter L., Price L., Gelernter J. Association between NGFB and affective disorder suggests potentially different genetic backgrounds between primary and drug dependence-comorbid affective disorders. The American Society of Human Genetics (ASHG) 58th Annual Meeting, November, 2008.
- A66. **Tyrka, A.R.**, Price, L.H., Kao, H.T., Porton, B., Marsella, S., and Carpenter, L.L. Reported Childhood Maltreatment Linked to Shortened Telomere Length in Healthy Adults: A Pilot Study. Brain Research Meeting: Stress, Coping and Disease, November, 2008.
- A67. Carpenter L.L., Lee J.K., **Tyrka A.R.**, Anderson G.M., Price L.H. Elevated IL-6 response to stress in healthy adults with early life adversity. Brain Research Meeting: Stress, Coping and Disease, November, 2008.
- A68. **Tyrka, A.R.**, Price, L.H., Kao, H.T., Porton, B., Marsella, S., and Carpenter, L.L. Reported Childhood Maltreatment Linked to Shortened Telomere Length in Healthy Adults: A Pilot Study. Annual Meeting of the American College of Neuropsychopharmacology, December 2008.

- A69. Carpenter L.L., Lee J.K., **Tyrka A.R.**, Anderson G.M., Price L.H. Elevated IL-6 response to stress in healthy adults with early life adversity. Annual Meeting of the American College of Neuropsychopharmacology, December 2008.
- A70. Malone, D.A.*, Dougherty, D.D.*, Rezai, A.R., Carpenter, L.L., Friehs, G.M., Eskander, E., Rauch, S.L., Rasmussen, S.A., Machado, A.G., Kubu, C.S., **Tyrka, A.R.**, Price, L.H., Stypulkowski, P.H., Giftakis, J., Malloy, P.F., Salloway, S.P., and Greenberg, B.D. Deep Brain Stimulation of the Ventral Capsule/Ventral Striatum for Treatment-Resistant Depression. American Psychiatric Association Annual Meeting, May 2009.

INVITED PRESENTATIONS

1. "Psychotic Depression." Butler Hospital Case Conference Series, 2/26/04, Regional Presentation.
2. "New Views on Women and Depression." Women and Infants Hospital Annual Women's Health Conference, 1/15/05, Regional Presentation.
3. "Risk for Depression: It's Nature *and* Nurture." Academic Meeting of the Butler Hospital Board of Trustees, 3/22/05, Regional Presentation.
4. "Sensitivity to Stress and Risk for Depression." Academic Presentation to the Butler Hospital Staff Association, 4/7/05, Regional Presentation.
5. "Clinical Psychiatry: Diagnosis and Management." Lecturer for Falcon Reviews, 6/05-5/06, National Presentation.
6. "Trauma and Psychopathology: Psychosocial and Biological Factors Influencing Risk and Resilience." Second Annual Joint Conference Butler Hospital and Family Service of Rhode Island, 3/24/06, Regional Presentation.
7. "Risk for Major Depression: Genes, Stress, and the HPA Axis," American Psychiatric Association 159th Annual Meeting, Toronto, May, 2006, National Presentation.
8. "Current Research and Significance of Childhood Trauma: Effects on Adulthood" . Women and Infants Hospital Annual Women's Health Conference, 5/15/07, Regional Presentation.
9. "Stress Sensitivity and Risk for Psychopathology: Genes, Experience and HPA Axis Function." Distinguished Faculty Speaker, Twelfth Annual Brown University Research Symposium, March, 2008, Regional Presentation.
10. "Corticotropin releasing hormone receptor (CRHR1) polymorphisms interact with early life stress to influence the cortisol response to the Dex/CRH test: Preliminary findings." Paper presented at the Annual Meeting of the Society of Biological Psychiatry, May, 2008, National Presentation.

11. "Neurobiology of Anxious Depression." American Psychiatric Association 162nd Annual Meeting, San Francisco, May 2009, National Presentation

GRANTS

1. 5 F30 MH10819-03 Predoctoral National Research Service Award, "Neuropsychological Indicators of Risk for Schizophrenia," Principal Investigator, 9/94-5/00.
2. NARSAD (Young Investigator Award), "Hypothalamic-Pituitary-Adrenal Function in Adults with a History of Early Life Stress," Principal Investigator; 6/03-5/05, \$60,000.
3. Janssen Pharmaceutica Faculty Development Award in Psychopharmacology, 5/18/03, \$25,000.
4. RSGPB PBP-103382 American Cancer Society, "Improving Smoking Cessation in Smokers with Depressive Symptoms", role: study physician, 7/02-6/04
5. Medtronic, Inc., "Electrical Stimulation of the Anterior Limb of the Internal Capsule to Treat Major Depressive Disorder," Co-Investigator, 10/02-9/04, \$315,000.
6. 1K23MH067947-1A1 Mentored Patient-Oriented Research Career Development Award, "Risk for Depression, Stress, and Neuroendocrine Function," Principal Investigator; 12/03-11/08, \$905,000.
7. Pfizer, Inc. "Sertraline Treatment and Cortisol Response to the DEX/CRH Test", Investigator-Initiated, Co-Investigator, 1/04-11/06, \$300,684.
8. United States Department of the Interior, "Perceived Early Life Stress and DEX/CRH Test Response as Predictors of Psychological Sequelae following Exposure of Healthy Adults to War Stress," Co-Investigator, 7/04-6/05, \$40,000
9. UCB Pharma, Inc. "Keppra Treatment and Cortisol Response to the DEX/CRH Test in Healthy Subjects," Investigator-Initiated, Co-Investigator, 6/04-5/07, \$111,624.
10. NCCAM/NIMH AT001742-01, "Double-blind, placebo-controlled study of SAME vs. escitalopram in MDD," Co-Investigator, 4/04 - 3/09, \$1,087,938.
11. United States Department of Defense, "Biomarkers of risk for post-traumatic stress disorder (PTSD)," Principal Investigator, 4/07-4/10, \$276,422.
12. Cyberonics, Inc. "Randomized Comparison of Outcomes in Patients with Treatment-Resistant Depression Who Receive VNS Therapy Administered at Different Amounts of Electrical Charge" Co-Investig; 11/1/07-present; \$230,000.
13. R01 MH0687670-01 "DEX/CRH Response: Mood/Anxiety Disorder Endophenotype? Phase 2." Co-Investigator, 12/08-11/13, \$3,514,780, pending.
14. R01 MH083704-01 "Childhood Maltreatment: Biomarkers of Risk and Resilience." Principal Investigator, 12/09-11/14, pending.
15. R01 MH086555-01 "Biomarkers of Risk and Resilience to Adversity." Principal Investigator, 7/01/09-6/30/14, pending,

16. R01 MH085838-01 “Onset and maintenance of PTSD in Iraq Veterans: a longitudinal study of psychosocial and biological risk factors.” Co-Principal Investigator, 12/01/09-11/01/14 pending, 3,907,421

UNIVERSITY TEACHING ROLES

Psychiatric Interviewing, PGY 1 Residents, 2003-present.

Introduction to Psychiatric Literature, PGY 1 Residents, 2003-2004

Mood Disorders Psychopharmacology lectures, PGY 1-4 Residents, 2003-present.

Mood Disorders Psychopathology lectures, PGY 1-4 Residents 2003-present .

Grant Reviewer, Post-doctoral fellows grantsmanship workshop 2004-2006

Research Supervisor, Post-Doctoral Psychology Fellows 2004-2007

Dissertation Committee Member, Pre-Doctoral Psychology Student 2005-2007

Course Director/Instructor, Principles of Biostatistics, T32 Post-Doctoral Fellows, 2006-2008

Morbidity and Mortality Conference Preceptor, PGY 1-4, 2007

Supervisor, Brown University Psychology Department senior student Independent Research Project 2007-2008

Supervisor, Brown University Neuroscience Concentrator senior student Independent Research Project 2008-2009

HOSPITAL TEACHING ROLES

Supervisor/preceptor, 3rd- and 4th-year Brown medical student clerks, 2003-2007

Supervisor, Brown psychiatry residents (Inpatient; PGY-1 - PGY-4), 2003-2007

Doctor-on-call supervisor, Butler Hosp. Patient Assessment Service, 2003-present.

Supervisor, Brown psychiatry residents (Outpatient, PG-3), 2003-present.